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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Mehran Khodadoust	Confirmation No.:	6131
Serial No.:	10/029,471	Art Unit:	1636
Filed:	October 25, 2001	Examiner:	Michele K. Joike
Customer No.:	21559		
Title:	COMPOSITIONS AND METHODS FOR THE DISCOVERY AND SELECTION OF BIOLOGICAL INFORMATION		

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicant respectfully requests review of the rejections set forth in the Office Action mailed on September 10, 2007 in connection with the above-captioned patent application. No amendments are being filed with this request and this request is being filed with a Notice of Appeal.

The review is requested for the reasons set forth below.

REMARKS

Claims 83-109 are pending. Claims 83, 84, and 88-96 stand twice rejected under 35 U.S.C. § 102(b) for anticipation by Baetscher et al., U.S.P.N. 5,922,601 ("Baetscher"). Claim 85, 86, 87, and 97-109 stand rejected under 35 U.S.C. § 103 for obviousness over Baetscher in view of MPEP § 2144.04 (VI)(C), Zambrowicz et al., U.S.P.N. 6,436,707 ("Zambrowicz"), or Massie et al. (*J. Virology* 72:2289-2296 (1998); "Massie"). All of these rejections are based on the assertion that Baetscher teaches all of the elements of the claims. Applicant disagrees.

Rejections under 35 U.S.C. § 102(b)

Claim 83 and several of its dependent claims stand rejected under § 102(b) as anticipated by Baetscher. The rejected claims are directed to nucleic acids, vectors, and cells that include promoterless constructs. Representative claim 83 is reproduced below.

> 83. A nucleic acid including:
> (a) a splice acceptor site;
> (b) a cassette including in any order a negative selection marker, a positive selection marker, and a reporter gene, wherein said negative selection marker, said positive selection maker, and said reporter gene are integrated into the genome of at least one cell and responsive to one or more endogenous regulatory elements in said at least one cell after said nucleic acid is contacted with a cell.

In rejecting claim 83, the Examiner asserts that

> Baetscher teaches integration of promoterless positive and negative selection markers (columns 4-6). Specifically a vector containing promoterless markers, including positive and negative selection markers, is integrated into the genome of a cell. The markers are promoterless so that once integrated, they are under control of an endogenous regulatory element." (Page 3, Office Action mailed on September 10, 2007; "the 2007 Office Action".)

For the following reasons, this conclusion mischaracterizes the Baetscher reference.

Baetscher never teaches a construct having a negative selection marker, positive selection marker, and reporter gene under the control of a host cellular promoter. Instead, Baetscher's constructs include two selection markers ***or*** a reporter gene and each of these include a promoter element regulating expression of the selection markers ***or*** reporter gene, but not all three.

The Examiner provides the rationale for the rejection by outlining the general formula of the constructs taught by Baetscher. Of these, the only constructs that include three markers, namely, a negative selection marker, a positive selection marker, and a reporter gene are those placed within the context of a retroviral vector. The Examiner summarizes the structures of Baetscher's constructs that include both positive and negative selection markers and the reporter gene as follows:

> Splice acceptor—IRES—positive selection—negative selection—STOP—***promoter***—reporter;
>
> Splice acceptor—IRES—Neo-HSV-TK—STOP—***promoter***—Ampicillin; and
>
> Splice acceptor—IRES—reporter—negative marker—STOP—***promoter***—positive marker. (Emphasis added.) (Pages 3-5, Office Action mailed on May 15, 2006; "the 2006 Office Action".)

Again, each of the constructs includes a promoter within the construct to drive expression of either the positive selection marker or the reporter, but a construct having a negative selection marker, positive selection marker, and reporter gene under the control of a host cellular promoter after contact with the host cell is never taught by Baetscher.

In contrast, Applicant's claimed constructs require that all three elements (i.e., the positive and negative selectable markers and the reporter gene) are under the control of an endogenous regulatory element in the host cell. Nowhere does the Examiner provide evidence that Baetscher teaches a construct having all three elements where all three elements are promoterless.

Applicant also notes, for the record, that there are inconsistencies in the Examiner's position, which despite Applicant's requests for an explanation remain unaddressed by the Examiner. For example, the Examiner states: "in order to get expression of the reporter, a promoter element must be operatively linked to the reporter gene" (Page 4, the 2006 Office Action) and then goes on to characterize Baetscher as teaching a construct having a splice acceptor site—IRES—positive selection—negative selection—reporter, all under the same

endogenous promoter of "a host cellular gene" (Page 6, the 2006 Office Action). The Examiner does not provide any explanation for the Office's interpretation of Baetscher or the inconsistencies in the Examiner's position throughout the 2006 Office Action.

In sum, all evidence of record indicates that Baetscher does *not* teach a nucleic acid construct that includes a negative selection marker, a positive selection marker, and a reporter gene where all three elements are integrated into the genome of a host cell and responsive to one or more endogenous regulatory elements in the host cell as recited in independent claim 83. In the absence of any evidence to the contrary, the anticipation rejection should be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 85, 86, 87, and 97-109 stand rejected under 35 U.S.C. § 103 for obviousness over Baetscher in view of MPEP § 2144.04 (VI)(C), Zambrowicz, or Massie. Each of the § 103 rejections relies on the teaching or suggestion by Baetscher of a construct where all of the selection markers and reporter gene are under control of at least one host cellular promoter (page 6 of the 2007 Office Action). As summarized above and as stated in the previous reply to the Office Action (dated June 15, 2007), Applicant's claimed constructs require that all three elements (i.e., the positive and negative selectable markers and the reporter gene) are responsive to endogenous regulatory elements of the host cellular gene and the advantages of having all three elements be promoterless and linked to endogenous regulatory elements of the host cellular gene are outlined in the June 15, 2007 reply at pages 7-9.

Applicant points out that the Examiner has relied on its § 102(b) grounds for rejecting the claims and has provided no separate reasoning for the obviousness of claims 85, 86, 87, and 97-109. To address this rejection, Applicant refers to the discussion above providing reasons for the novelty of the claimed constructs and the discussion of Baetscher. This discussion explains that Applicant's claimed inventions are not provided by the art. In the absence of a teaching or suggestion of Applicant's claimed nucleic acid construct, the art similarly cannot provide the claimed nucleic acids, vectors, or cells that include all the features of the claimed nucleic acid construct. In addition, Applicant points out that the secondary references—MPEP § 2144.04 (VI)(C), Zambrowicz, and Massie—add nothing of significance because each of these references

fails to provide any insight into the features of the nucleic acid construct taught by Applicant. The secondary references are merely cited for showing that rearrangement of parts is an obvious modification (MPEP), that a recombinase site can be included in a nucleic acid construct (Zambrowicz), and that a transactivator can be included in a nucleic acid construct (Massie). Accordingly, because the secondary references do not provide a nucleic acid construct that includes a negative selection marker, a positive selection marker, and a reporter gene where all three elements are responsive to one or more endogenous regulatory elements in the host cell, they cannot render claims 85, 86, 87, and 97-109 obvious.

Applicants request reconsideration on this issue and withdrawal of the § 103 rejection.

CONCLUSION

Applicant submits that the application is in condition for allowance, and this action is hereby respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: February 11, 2008

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